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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/808,541	03/25/2004	Abraham Nudelman	27755	4875

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/808,541	NUDELMAN ET AL.	
	Examiner	Art Unit	
	Brenda L. Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-125* is/are pending in the application.

4a) Of the above claim(s) *12-14,16-25,35-37,54-56,72-74,89-91,97 and 99-116* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,15,26-34,38-53,57-71,75-88,92-96,98 and 117-125* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

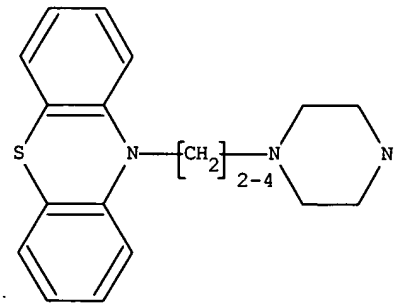
Claims 1-125 are pending in the application.

Election/Restrictions

1. Applicant's election of Perphenazine 4-aminobutyrate trihydrochloride in the reply filed on May 1, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The applicants' indication of the claims which they believed read on the species is accepted at this time, however, if upon further review or examination during the prosecution of the application it is found that a claim does not in fact read on the species that claim will therefore be withdrawn.

2. Applicants' are advised that the compounds of claim 1 have only been examined to the extent that the species contain the perphenazine core, i.e.



3. Claims 12-14, 16-25, 35-37, 54-56, 72-74, 89-91, 97 and 99-116 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected

invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 1, 2006.

Specification

4. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-11, 15, 26-34, 38-53, 57-71, 75-88, 92-96, 98 and 117-125 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the species in the specification of examples AN-130, AN-167, AN-168, AN-177, AN-178, AN-180, AN-179, AN-181, AN-187 and AN-216, does not reasonably provide enablement for the compounds, compositions, method of use and process of preparing

the compounds as claimed herein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

HOW TO MAKE: In evaluating the enablement question, several factors are to be considered. *In re* Wands, 8 USPQ2d 1400 (Fed. Cir. 1988); *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant case, has claims which embrace compounds where a first chemical moiety is a psychotrophic drug and the second chemical moiety is an organic acid residue of which the applicants have neither supported or contemplated.

The instant specification teaches about 9 examples where the "psychotrophic drug" is the perphenazine core. Each of these examples only possesses a tricyclic ring system substituted by a piperazinylalkyl moiety on the nitrogen atom of the perphenazine core.

HOW TO USE: The scope of "psychotrophic disorder or disease", neurodegenerative disease or disorder", "proliferative disorder or disease", "cancer" or "multidrug resistant cancer" cannot be deemed enabled. The notion that a compound could be effective against psychotrophic, neurodegenerative or proliferative disorder or disease, cancer or multidrug resistant cancer in general is contrary to our current

understanding of how pharmacologicals work. All attempts to find a pharmaceutical to treat psychotrophic, neurodegenerative or proliferative disorder or disease, cancer or multidrug resistant cancer generally have thus failed. Additionally, instant claim language embraces disorders not only for treatment but for prevention which is not remotely enabled.

In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention. To be enabling, the specification of a patent must teach those skilled in the art how to make and use the scope of the claimed invention without undue experimentation. The applicants' are not entitled to preempt the efforts of others. The test for determining compliance with 35 U.S.C. § 112, is whether the applicants have clearly defined their invention.

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague information of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. Genentech Inc. v. Novo Nordisk 42 USPQ2d 1001.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 1-11, 15, 26-34, 38-53, 57-71, 75-88, 92-96, 98 and 117-125 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly

point out and distinctly claim the subject matter which applicant regards as the invention. The following reason(s) apply:

a) Claims 1-11, 15, 26-34, 38-53, 57-71, 75-88, 92-96, 98 and 117-125 are vague and indefinite in that it is not known what is meant by the "psychotrophic drug residue", which does not set forth the metes and bounds of the claim.

b) Claims 1-11, 15, 26-34, 38-53, 57-71, 75-88, 92-96, 98 and 117-125 are vague and indefinite in that it is not known what is meant by the "organic acid residue", which does not set forth the metes and bounds of the claim.

c) Claims 1-11, 15, 26-34, 38-53, 57-71, 75-88, 92-96, 98 and 117-125 are vague and indefinite in that it is not known what is meant by the "reduce side effects". Which fails to set forth the degree or kind such that the following questions may be answered: Which side effects? Reduced how much? Where does it teach how to measure?

d) Claims 2, 44, 62, 79, 94, 117 and 119 are vague and indefinite in that it is not known what is meant by the "GABA agonist residue", which does not set forth the metes and bounds of the claim.

e) Claims 2, 44, 62, 79 and 94 are vague and indefinite in that it is not known what is meant by the "analgesic residue", which does not set forth the metes and bounds of the claim.

f) Claims 2, 44, 62, 79 and 94 are vague and indefinite in that it is not known what is meant by the "anti-proliferative agent residue", which does not set forth the metes and bounds of the claim.

g) Claims 4, 27, 46, 64 and 81 are vague and indefinite in that it is not known what is meant by "anti-proliferative activity".

h) Claims 5, 28, 47, 65 and 82 are vague and indefinite in that it is not known what is meant by "chemosensitization activity".

i) Claims 7, 30, 49, 67, 84 and 121 are vague and indefinite in that it is not known what is meant by the "anti-psychotic drug residue", which does not set forth the metes and bounds of the claim.

j) Claims 8, 31, 50, 68, 85 and 122 are vague and indefinite in that it is not known what is meant by the "typical anti-psychotic drug residue or atypical psychotic drug residue", which does not set forth the metes and bounds of the claim.

k) Claims 9, 32, 51, 69, 86 and 123 are vague and indefinite in that it is not known what is meant by the "anxiolytic drug residue, an anti-depressant residue, an anti-convulsive drug residue, an anti-parkinsonian drug residue, an acetylcholine esterase inhibitor residue, a MAO inhibitor residue. a tricyclic psychotropic drug residue, a bicyclic psychotropic drug residue, a monocyclic psychotropic drug residue, a phenothiazine residue, a benzodiazepine residue and a butyrophenone residue", which does not set forth the metes and bounds of the claim.

l) Claims 10, 33, 52, 70, 87 and 124 are vague and indefinite in that it is not known what is meant by the "chloropromazine residue, a perphenazine residue, a fluphenazine residue, a zuclopenthixol residue, a thiopropazate residue, a

haloperidol residue, a benperidol residue, a bromperidol residue, a droperidol residue, a spiperone residue, a pimozide residue, a piperacetazine residue, an amilsulpride residue, a sulpiride residue, a clothiapine residue, a ziprasidone residue, a remoxipride residue, a sultopride residue, an alizapride residue, a nemonapride residue, a clozapine residue, an olanzapine residue, a ziprasiidone residue, a sertindole residue, a quetiapine residue, a fluoxetine residue, a fluvoxamine residue, a desipramine residue, a paroxetine residue, a sertraline residue, a valproic acid residue, a temazepam residue, a flutemazepam residue, a doxefazepam residue, an oxazepam residue, a lorazepam residue, a lormetazepam residue, a cinolazepam residue, a flutazolam residue, a lopirazepam residue, a meprobamate residue, a carisoprodol residue. an acetophenazine residue, a carphenazine residuc, a dixyrazine residue, a priciazine residue, a pipothiazine residue, a homophenazine residue, a perimetazine residue, a perthipentyl residue, a flupentixol residue, a piflutixol residue, a teflutixol residue, an oxypethepin residue, trifluperidol residue, a penfluridol residue, a meclobemide residue, a norclomipramine residue, an amoxapinc residue, a nortriptyline residue, a protriptyline rcsidue, a reboxetine residue, a tacrine residue, a rasagiline residue, an amatadine residue, a phenobarbital residue and a phenytoin residue", which does not set forth the metes and bounds of the claim.

m) Claims 11, 34, 53, 71, 88 and 119 are vague and indefinite in that it is not known what is meant by the "(±) baclofen residue, an γ-aminobutyric acid

(GABA) residue, a γ-hydroxybutyric acid residue, an aminooxyacetic acid residue, a β-(4-chlorophenyl)-γ-aminobutyric acid residue, an isonipecotic acid residue, a piperidine-4-sulfonic acid residue, 3-aminopropylphosphonous acid residue, an 3-aminopropylphosphinic acid residue, an 3-(aminopropyl)metllylphosphinic acid residue, a 1-(aminomethyl)cyclohexaneacetic acid residue (gabapentin), A γ-vinyl-γ-aminobutyric acid (γ-vinyl GABA, vigabatrin) and an 3-(2—imidazolyl)-4-aminobutanoic acid residue", which does not set forth the metes and bounds of the claim.

n) Claims 15, 38, 57, 75, 92 and 125 are vague and indefinite in that it is not known what is meant by the "a butyric acid residue, a valeric acid residue, a 4-phenylbutyric acid residue, an 4-aminobutyric acid residue, a retinoic acid residue, a sulindac acid residue, an acetyl salicylic acid residue, an ibuprofen residue, a malonic acid residue, a succinic acid residue, a glutaric acid residue, a fumaric acid residue and a phthalic acid residue", which does not set forth the metes and bounds of the claim.

o) Claim 76 is vague and indefinite in that it is not known what is meant by the "chemosensitization, in combination with a chemotherapeutic agent and/or in a medical condition for which chemosensitization is beneficial", which does not set forth the metes and bounds of the claim.

p) Claims 93-96, 98 and 117-125 are vague and indefinite in that it is not known what is meant by the "psychotropic drug", which does not set forth the metes and bounds of the claim.

q) Claim 98 is vague and indefinite in that it is not known what is meant by the "anti-proliferative agent", which does not set forth the metes and bounds of the claim.

r) Claims 95 and 98 are vague and indefinite in that it is not known what is meant by "acyl chloride derivative" which implies more then what is positively recited.

s) Claim 98 is vague and indefinite in that it is not known what is meant by "thiol derivative" which implies more then what is positively recited.

t) Claim 118 is vague and indefinite in that it is not known what is meant by "acyl imidazole derivative" which implies more then what is positively recited.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-11, 15, 26-34, 38-53, 57-71, 75-88, 92-96, 98 and 117-125 are rejected under 35 U.S.C. 102(e) as being anticipated by Borisy et al., U.S. 6,569,853. Borisy

teaches the elements of the applicants elected compounds such that the perphenazine ring as set forth by formula B-3 where the perphenazine ring is substituted by $-C(O)CH_3$ or $-C(O)-(CH_2)_5-CH_3$ and the compounds are for the same uses as claimed herein. See RN 84-06-0 and 17528-28-8.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brenda Coleman

Brenda L. Coleman
Primary Examiner Art Unit 1624
July 21, 2006